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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/809,631	03/24/2004	Nathan Andrew Shapira	UF-368XC1	8943

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EXAMINER	
WANG, SHENGJUN	
ART UNIT	PAPER NUMBER
1617	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/809,631	SHAPIRA ET AL.	
	Examiner	Art Unit	
	Shengjun Wang	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 October 2008*.

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,6,7,11-15,18,19,23,24,32-34,37,38 and 42-47* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,6,7,11-15,18,19,23,24,32-34,37,38 and 42-47* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/17/2008 has been entered.

Claim Rejections 35 U.S.A. 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. Claims 1-3, 6-7, 13-15, 18-19, 32-34, 37-38, 44-47 are rejected under 35 U.S.C. 103(a) as being unpatentable over Waldinger et al. (NL 1012954, and Maturitas, 2000, vol. 36, pages 165-168), in further view of Andrews et al. (WO 01/52855).

3. Waldinger et al. teaches a method of treating patients suffering hot flushing and perspiration with mirtazapine. See, the abstract of NL 1012954 and Maturitas. Waldinger et al. discloses that mirtazapine is particularly effective in alleviating perspiration. See, particularly the cases in Maturitas.

4. Waldinger et al. do not teach expressly the treatment of primary hyperhidrosis or idiopathic hyperhidrosis, or the particular dosage form of mirtazapine.

However, it would have been prima facie obvious to a person of ordinary skill in the art, at the time the claimed the invention was made, to treat idiopathic hyperhidrosis patients with mirtazapine for alleviating perspiration.

A person of ordinary skill in the art would have been motivated treat idiopathic hyperhidrosis patients for alleviating perspiration with mirtazapine because mirtazapine is known to be useful in alleviating perspiration. One of ordinary skill in the art would have reasonably expected that mirtazapine would be symptomatically useful for treating perspiration caused by any etiologies as it has been shown that mirtazapine is particularly effective in alleviating perspiration. Further, Andrews reveals that mirtazapine is an old and well-known therapeutical agent and may be formulated to conventional dosage forms for oral, parenteral, topical administrations. See, particularly, page 1, lines 16-19, page 8, line 4-38. Therefore, making a particular dosage form, such as liposome, or selecting a particular administration method for mirtazapine would have been within the purview of ordinary skill in the art. Finally, it is noted that perspiration for patient with hyperhidrosis happens periodically, the treatment as disclosed by Waldinger et al. do not require the administration be carried out at the time of perspiration, therefore, would meet the limitation "prophylactically" recited in claims 32.

Claims 1-3, 6-7, 13-15, 18-19, 32-34, 37-38, 44-47 are rejected under 35 U.S.C. 103(a) as being unpatentable over Waldinger et al. (NL 1012954, and Maturitas, 2000, vol. 36, pages 165-168), in view of Davidson et al. (IDS), and in further view of Andrews et al. (WO 01/52855).

5. Waldinger et al. teaches a method of treating patients suffering hot flushing and perspiration with mirtazapine, a serotonin antagonist. See, the abstract of NL 1012954 and

Maturitas. Waldinger et al. discloses that mirtazapine is particularly effective in alleviating perspiration. See, particularly the cases in Maturitas.

6. Waldinger et al. do not teach expressly the treatment of primary hyperhidrosis or idiopathic hyperhidrosis.

However, Davidson teaches that fluoxetine an antidepressant and serotonin antagonist is effective for reduce the symptoms of hyperhidrosis in patients of social anxiety disorders and suggest serotonergic mechanism is associated with the hyperhidrosis. See, particularly, the abstract at page 1327, and the discussion and conclusion at pages 1330-1331.

Therefore, it would have been prima facie obvious to a person of ordinary skill in the art, at the time the claimed the invention was made, to treat idiopathic hyperhidrosis patients with serotonin antagonist, such as mirtazapine for alleviating perspiration.

A person of ordinary skill in the art would have been motivated to treat idiopathic hyperhidrosis patients for alleviating perspiration with mirtazapine because serotonin antagonists, mirtazapine in particular, are known to be useful in alleviating perspiration. One of ordinary skill in the art would have reasonably expected that mirtazapine would be symptomatically useful for treating perspiration caused by any etiologies as it has been shown that mirtazapine is particularly effective in alleviating perspiration. Further, Andrews reveals that mirtazapine is an old and well-known therapeutical agent and may be formulated to conventional dosage forms for oral, parenteral, topical administrations. See, particularly, page 1, lines 16-19, page 8, line 4-38. Therefore, making a particular dosage form, such as liposome, or selecting a particular administration method for mirtazapine would have been within the purview of ordinary skill in the art. Finally, it is noted that perspiration for patient with hyperhidrosis

happens periodically, the treatment as disclosed by Waldinger et al. do not require the administration be carried out at the time of perspiration, therefore, would meet the limitation "prophylactically" recited in claims 32.

7. Claims 11, 12, 23, 24, 42, and 43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Waldinger et al. (NL 1012954, and Maturitas, 2000, vol. 36, pages 165-168), in further view of Andrews et al. (WO 01/52855) for reasons discussed above, and in further view of Saadia et al. (IDS).

Waldinger et al. and Andrews as a whole do not teach expressly the further injection of botulinum.

However, Saadia et al. teaches that local intradermal injection of botulinum is known to be useful for treating hyperhidrosis.

Therefore, it would have been prima facie obvious to a person of ordinary skill in the art, at the time the claimed the invention was made, to further incorporate a step of injection botulinum for treatment of hyperhidrosis.

A person of ordinary skill in the art would have been motivated to further incorporate a step of injection botulinum for treatment of hyperhidrosis because it is prima facie obvious to combine two compositions each of which is taught in the prior art to be useful for same purpose in order to form third composition (or method of using the same) that is to be used for very the same purpose; idea of combining them flows logically from their having been individually taught in prior art; See In re Kerkhoven, 205 USPQ 1069.

8. Claims 11, 12, 23, 24, 42, and 43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Waldinger et al. (NL 1012954, and Maturitas, 2000, vol. 36, pages 165-168),

in view of Davidson et al. (IDS), and in further view of Andrews et al. (WO 01/52855) for reasons discussed above, and in further view of Saadia et al. (IDS).

Waldinger et al. Davidson et al. and Andrews as a whole do not teach expressly the further injection of botulinum.

However, Saadia et al. teaches that local intradermal injection of botulinum is known to be useful for treating hyperhidrosis.

Therefore, it would have been prima facie obvious to a person of ordinary skill in the art, at the time the claimed the invention was made, to further incorporate a step of injection botulinum for treatment of hyperhidrosis.

A person of ordinary skill in the art would have been motivated to further incorporate a step of injection botulinum for treatment of hyperhidrosis because it is prima facie obvious to combine two compositions each of which is taught in the prior art to be useful for same purpose in order to form third composition (or method of using the same) that is to be used for very the same purpose; idea of combining them flows logically from their having been individually taught in prior art; See In re Kerkhoven, 205 USPQ 1069.

Response to the Arguments

Applicants' remarks submitted October 17, 2008 have been fully considered, but are not persuasive.

Applicants again contend that the claimed invention would have not been obvious over the cited references because the cited references teach expressly the treatment of symptoms with distinct underline etiologies. The examiner respectfully disagrees and maintains his position as discussed in the prior office action.

9. With respect to the rejection under 35 U.S.C. 103 over Waldinger et al. in view of Andrews et al. (WO 01/52855), applicants contend that skilled artisan would have not expected mirtazapine be useful in treatment of perspiration by other etiologies because Waldinger teach mirtazapine for treatment of hot flash only. The arguments are not persuasive. Applicants' attention is directed to the abstract of Waldinger (Maturitas, or Waldinger II), where it states:

Conclusion: Mirtazapine appears to have a substantial ameliorating effect on hot flushes *and perspiration bouts.* It is postulated that the 5-$HT2_A$ blocking properties of mirtazapine is accounted in the symptomatic relief of hot flushes. In addition it is hypothesized that the serotonergic system is crucially involved in the pathogenesis of hot flushes *and perspiration* bouts. (emphasis added).

It is clear to an ordinary skill in the art that Mirtazapine is useful for symptomatically release of perspiration.

With respect to the rejection under 35 U.S.C. 103 over Waldinger et al. in view of Davidson et al. (IDS), and in further view of Andrews et al. (WO 01/52855), applicants argue that Davidson reference fails to teach method for treating idiopathic hyperhidrosis. It is noted that Davidson teaches that fluoxetine an antidepressant and serotonin antagonist is effective for reduce the symptoms of hyperhidrosis in patients of social anxiety disorders and suggest serotonergic mechanism is associated with the hyperhidrosis. Therefore, considering the cited references as a whole, it would have been obvious to use mirtazapine, a well-known serotonin antagonist, for treatment of hyperhidrosis.

10. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Particularly, the cited references

as a whole have fairly suggested the usefulness of mirtazapine, as well as other 5-HT2 receptor antagonist, for symptomatically ameliorating hyperhidrosis.

11. Applicants' rebuttal comments argue a different etiology between the prior art hyperhidrosis and that claimed herein. Applicants argue that a linkage to declining estrogen levels as a condition underlying the etiology patentably distinguishes an otherwise identical syndrome. It is well-settled fact that in treating syndromes, therapy is directed to alleviating symptomology. That eliminating the underlying etiology results in disease suppression is well known to the skilled artisan. Similarly, faced with a disease state, the skilled artisan would have been motivated to treat these symptoms with medicaments old and well known to treat the disease state; regardless the underlying etiology. Thus regardless the etiology, to treat hyperhidrosis symptomatically with old and well-known serotonin agents would have been obvious to the normal skilled artisan.

12. In response to applicant's argument that the claimed invention pertains to the use of the compound to affect 5-HT2C, the fact that applicant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious. See *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985). It is noted that the cited references suggest the same compound, mirtazapine, for treating hyperhidrosis. Applicants' recognition of affecting 5-HT2C, as oppose to 5-HT2A, would not make the claimed invention distinct.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shengjun Wang whose telephone number is (571) 272-0632. The examiner can normally be reached on Monday to Friday from 7:00 am to 3:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Shengjun Wang/
Primary Examiner, Art Unit 1617

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